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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,763	01/16/2002	Su-May Yu	08919-067001 / 13A-900806	7868

26161 7590 07/03/2003

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EXAMINER
FOX, DAVID T

ART UNIT	PAPER NUMBER
1638	11

DATE MAILED: 07/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/050,763	Yu et al
Examiner	**Group Art Unit**
FOX	1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE -3- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 4/23/03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 1-47 is/are pending in the application.

Of the above claim(s) 37-47 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-36 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other _____

Office Action Summary

Applicant's election without traverse of Group I in Paper No. 10 is acknowledged.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 5-13, 16-29 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any nucleotide sequence of any sequence and from any source (including any bacterial species, any fungal or viral species, any plant species, or any animal species) which encodes amylopullulanase, or any nucleotide sequence encoding any fragment thereof of any length or sequence. In contrast, the specification only provides guidance for a single microbial amylopullulanase gene from a single bacterial species, and a single fragment thereof. No guidance is provided regarding any other source of amylopullulanase gene or fragment.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California* v. *Eli Lilly and Co.*, 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that

"naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." *Id.* Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." *Id.*

See MPEP Section 2163, page 156 of Chapter 2100 of the August 2001 version, column 2, bottom paragraph, where it is taught that

> [T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111).

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

See also *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Claims 1-2, 5-13, 16-29 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a nucleotide sequence from Thermoanaerobacter ethanolicus which encodes pullulanase, or a particular truncation thereof which does not encode amino acids 1-105 or 1061-1481 of the enzyme, and plants transformed therewith; does not reasonably provide enablement for claims broadly drawn to any nucleotide sequence from any source and sequence which encodes any amylopullulanase of any sequence, or any fragment thereof, or their use to alter starch in plants transformed therewith. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to any nucleotide sequence of any sequence and from any source (including any bacterial species, any fungal or viral species, any plant species, or any

animal species) which encodes amylopullulanase, or any nucleotide sequence encoding any fragment thereof of any length or sequence. The claims are also drawn to methods of using the sequences to transform plants for modified starch content or composition. In contrast, the specification only provides guidance for a single microbial amylopullulanase gene from a single bacterial species, and a single fragment thereof. No guidance is provided regarding any other source of amylopullulanase gene or fragment.

The isolation and truncation of amylopullulanase genes is unpredictable. Ramesh et al teach that amylopullulanase enzymes only occur in a few thermoanaerobic bacteria, and that deletions of amino acid residues greatly reduces thermal stability of the enzyme (see, e.g., page 94, column 1; page 100, column 2, top paragraph).

The process of modifying starch accumulation in transgenic plants is particularly unpredictable. See Kossmann et al (1995; Progress in Biotechnology, Volume 10), who teach the lack of influence of antisense potato starch accumulation genes on branching or phosphate content of starch (page 275, third through fifth full paragraphs), the difficulty inherent in isolating individual starch synthesis enzymes or their corresponding genes (paragraph bridging pages 275 and 276), and the lack of correlation between reduction of branching enzyme gene activity and branching of starch in transgenic plants (see, e.g., page 277, penultimate paragraph).

Given the unpredictability, claim breadth, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify and isolate a multitude of non-exemplified amylopullulanase genes from a multitude of non-exemplified

bacterial or non-bacterial sources, and to evaluate the ability of these sequences or a multitude of fragments thereof for their ability to alter starch content or composition in plants transformed therewith.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4, 14-15, 30-31 and 35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in their recitation of "T." as it is unclear which genus of which organism is intended. Replacement of the first recitation of "T." in claim 3 with -- *Thermoanaerobacterium*-- would obviate this rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-36 are rejected under 35 U.S.C. 102(a) as being anticipated by EP 1,164,194 (ACADEMIA SINICA).

The claims are drawn to rice plant transformation with a DNA construct comprising a seed-specific promoter including the glutelin promoter or an alpha-amylase-3 or -8 promoter, ligated to an amylopullulanase gene from *T. ethanolicus* including any fragment thereof which

does not encode all of amino acids 1-105 or 1061-1481, and a method for extracting starch from the transformed plants.

ACADEMIA SINICA teaches rice plant transformation with a DNA construct comprising the *T. ethanolicus* amylopullulanase gene which has been truncated to not encode amino acids 1-74 or 1030-1481, ligated to either the glutelin-1 promoter or the alpha-amylase-8 promoter, and starch extraction from the transgenic rice seeds (see, e.g., pages 2-11).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 5, 7-9, 11-13, 16, 20, 22-25, 27, 29, 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barry et al (U.S. 5,750,876) taken with Duffner (U.S. 6,043,074).

The claims are drawn to corn plant transformation with a DNA construct comprising a seed-specific promoter including the glutelin promoter, ligated to a signal peptide-encoding sequence and a microbial amylopullulanase gene, and a method for extracting modified starch from the transformed plants.

Barry et al teach corn plant transformation with an isoamylase gene for the alteration of starch content or composition, wherein isoamylase and pullulanase are enzymes involved in starch debranching, under the control of a signal sequence and a glutelin promoter, and suggest the use of seed-specific promoters for those crops which store starch in their seeds including corn (see, e.g., column 1, line 65 through column 2, line 14; column 2, lines 33-43; column 3, lines 33-39; column 10, lines 9-15 and 28-37; column 11, lines 1-20; column 16, line 57 through column 18, line 20; claims 10-12. 17-19, 22, and 24-26).

Barry et al do not teach plant transformation with an amylopullulanase gene.

Duffner teach a microbial amylopullulanase gene encoding an enzyme which is useful in starch processing and which is stable at high temperatures, bacterial transformation with the gene, and suggests plant transformation therewith (see, e.g., column 1, lines 20-27, 37-55; column 3, lines 10-14; column 15, lines 54-55; column 20, line 43 through column 22, line 10).

It would have been obvious to one of ordinary skill in the art to utilize the method for plant transformation with a glutelin promoter ligated to a starch-modification gene such as an isoamylase gene as taught by Barry et al, and to modify that method by incorporating the amylopullulanase gene taught by Duffner, as suggested by Duffner, given the recognition by one of ordinary skill in the art that choice of starch-modifying enzyme would have been the optimization of process parameters.

Claims 17-18, 28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barry et al (U.S. 5,750,876) in view of Duffner (U.S. 6,043,074) as applied to claims 1-2, 5, 7-9, 11-13, 16, 20, 22-25, 27, 29, 32 and 34 above, and further in view of Maruta (U.S. 5,516,668).

The claims are drawn to rice plant transformation with a DNA construct comprising a seed-specific promoter including the glutelin promoter, ligated to a signal peptide-encoding sequence and a microbial amylopullulanase gene, and a method for extracting modified starch from the transformed plants.

Barry et al taken with Duffner teach corn plants transformed with the glutelin promoter ligated to a microbial amylopullulanase gene for the alteration of starch extracted from the corn seed, and Barry et al also suggest the use of other starch-accumulating plants such as rice (see, e.g., column 3, lines 33-38).

Barry et al taken with Duffner do not actually teach rice plants transformed with an amylopullulanase gene.

Maruta teaches a method for rice plant transformation with the glutelin promoter and whole plant regeneration, wherein the method may be used for the production of foreign proteins in rice seeds (see, e.g., column 4, line 63 through column 5, line 44; column 5, line 64 through column 6, line 40).

It would have been obvious to one of ordinary skill in the art to utilize the method of cereal plant transformation with a DNA construct comprising a glutelin promoter and a microbial amylopullulanase gene as taught by Barry et al taken with Duffner, and to modify that method by incorporating the rice transformation method taught by Maruta, as suggested by Barry et al.

Claims 6 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barry et al (U.S. 5,750,876) in view of Duffner (U.S. 6,043,074) as applied to claims 1-2, 5, 7-9, 11-13, 16, 20, 22-25, 27, 29, 32 and 34 above, and further in view of Leisy et al.

The claims are drawn to corn plant transformation with a DNA construct comprising a seed-specific promoter including the glutelin promoter, ligated to a glutelin signal peptide-encoding sequence and a microbial amylopullulanase gene, and a method for extracting modified starch from the transformed plants.

Barry et al taken with Duffner teach corn plants transformed with the glutelin promoter ligated to a signal sequence ligated to microbial amylopullulanase gene for the alteration of starch extracted from the corn seed, as stated above.

Barry et al do not teach a glutelin signal sequence.

Leisy et al teach plant transformation with a DNA construct comprising the glutelin promoter and glutelin signal sequence (see, e.g., page 41, Abstract; page 43, Figure 1).

It would have been obvious to one of ordinary skill in the art to utilize the method of cereal plant transformation with a DNA construct comprising a glutelin promoter, a signal sequence and a microbial amylopullulanase gene as taught by Barry et al taken with Duffner, and to modify that method by incorporating the glutelin signal sequence taught by Leisy et al, given the recognition by those of ordinary skill in the art that choice of source or sequence of signal sequence would have been the optimization of process paremeters.

Claims 1-2, 5, 7-10, 12-13, 16-18, 20, 22-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rodriguez (U.S. 5,888,789) taken with Duffner (U.S. 6,043,074).

The claims are drawn to rice seeds transformed with a DNA construct comprising a seed-specific alpha amylase promoter including an alpha-amylase-3 promoter ligated to a signal sequence ligated to a microbial amylopullulanase gene.

Rodriguez teaches rice transformation with a DNA construct comprising a seed-specific alpha-amylase-1 or -3 promoter ligated to an alpha-amylase signal sequence for the production of useful peptides in rice seeds (see, e.g., column 3, lines 28-46 and 54-67; column 4, lines 32-39; column 10, lines 28-38; column 12, lines 8-67; column 15, lines 1-45; column 33; column 34, line 55 through column 35, line 8).

Rodriguez does not teach the use of an amylopullulanase gene.

Duffner teaches the advantages of amylopullulanase enzymes and suggests plant cell transformation with the genes encoding them for the production of the enzyme, as discussed above.

It would have been obvious to one of ordinary skill in the art to utilize the method of producing desired proteins in rice seeds via transforming rice with a DNA construct comprising a seed-specific alpha-amylase promoter including the alpha-amylase-3 promoter, and to modify that method by incorporating the amylopullulanase gene taught by Duffner, as suggested by each reference.

Claims 1-5, 7-9, 11-20, 22-25 and 27-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barry et al (U.S. 5,750,876) taken with Maruta (U.S. 5,516,668), Mathupala et al, Zeikus et al, and Chiang et al (July 2001).

The claims are drawn to rice transformation with a DNA construct comprising a seed-specific glutelin promoter ligated to a signal sequence ligated to a full-length or truncated *T. ethanolicus* amylopullulanase gene, for the production of modified starch.

Barry et al teach cereal transformation with a DNA construct comprising a glutelin promoter ligated to a signal sequence and an isoamylase gene for the production of altered starch in the cereal seed, and also suggest rice transformation, as discussed above.

Barry et al do not teach rice transformation or a full-length or truncated *T. ethanolicus* amylopullulanase gene.

Maruta teaches rice transformation with a glutelin promoter as discussed above.

Mathupala et al teach the cloning of the *T. ethanolicus* amylopullulanase gene (see, e.g., pages 16332-1633 and pages 16336-16341).

Zeikus et al teach that truncation of the first 106 amino acids of the *T. ethanolicus* amylopullulanase increased the half-life of the enzyme, and that truncation of the first 106 and last 247 amino acids did not change optimum temperature or half-life of the enzyme (see, e.g., page 259, Figure 7).

Chiang et al report that rice seeds transformed with a DNA construct comprising a glutelin promoter ligated to a signal sequence and a truncated *T. ethanolicus* amylopullulanase gene produced usefully altered forms of starch (see Abstract).

It would have been obvious to one of ordinary skill in the art to utilize the method of cereal transformation with a gene encoding a starch-synthesis enzyme under the control of the seed-specific glutelin promoter as taught by Barry et al, to modify that method by utilizing the rice transformation method taught by Maruta as suggested by Barry et al, and to further modify that method by incorporating either the full-length *T. ethanolicus* amylopullulanase gene taught by Mathupala et al or the truncated gene taught by Zeikus et al, given the suggestion to do so by Chiang et al.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 30, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638